

Application Serial No. 09/981,289  
Filing Date: October 15, 2001

### REMARKS

Claims 50- 72 are pending. Claims 50, 58, 59, 64, and 70-72 have been amended. Claims 1-49 have been cancelled.

Applicants respectfully thank the Examiner for the telephone conference of November 28, 2005, in which the amendments were discussed.

Applicants have amended the claims to refer to "amino acids 1-157 of SEQ ID NO:2" instead of "SEQ ID NO:2." Support for the absence of a His-tag in naturally occurring TNF- $\alpha$  is found, for example, in the description of Fig. 6B at page 3, lines 21-23 of the specification, which makes it clear that a His-tag and start codon are before the first amino acid of the naturally occurring TNF- $\alpha$  sequence. One of skill in the art would readily recognize that a naturally occurring TNF- $\alpha$  sequence would not include an N-terminal His-tag.

In accordance with M.P.E.P. § 714.16(a), Applicants respectfully state the following:

(A) The pending claims are directed to a variant TNF- $\alpha$  protein comprising an amino acid substitution of SEQ ID NO: 2. However, the referenced SEQ ID NO:2 includes an N-terminal methionine His-tag on the naturally-occurring TNF- $\alpha$ . The naturally-occurring TNF- $\alpha$  corresponds to amino acids 1-157 of SEQ ID NO:2.

(B) The proposed amendment does not require any additional search because it appears that the search was conducted over the naturally occurring TNF- $\alpha$  sequence. In the Office Action of May 19, 2003, for example, the search resulted in a rejection over U.S. Patent No. 5,597,899 to Banner et al. Banner et al. does not disclose naturally occurring sequence including methionine-His tag. The Patent Office thus appears to have searched only the portion of SEQ ID NO:2 that includes the naturally occurring TNF- $\alpha$  sequence, and not the methionine His-tag.

(C) The claims are patentable over the prior art. Further, all issues under 35 U.S.C. § 112 have been addressed during prosecution.

(D) The claims were not presented in their current form earlier because the Applicant believed that SEQ ID NO:2 included only the naturally occurring TNF- $\alpha$  sequence.

Applicants respectfully request entry of the present amendment.

If a telephone conference would assist the prosecution of this application, Applicants respectfully request that the Examiner contact the undersigned at (415) 781-1989.

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Please direct any calls in connection with this application to the undersigned at (415)  
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Respectfully submitted,  
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